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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/300,482	04/28/1999	NORDINE CHEIKH	04983.0031.U	4511

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IP DOCKETING DEPARTMENT; RM 1126(b)
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EXAMINER
MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/300,482	CHEIKH ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,10-13,15-22 and 24-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10-13,15-22 and 24-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and rejections not repeated below are hereby withdrawn. Claims 1-2, 10-13, 15-22, and 24-31 are pending.

Priority

Applicant is reminded that priority is granted to the filing of the Provisional application (filed 4/29/1998) for claims reciting only 1, 225, and 619, as set forth in the office action of 7/17/02. SEQ ID NO's 4, 14, 27, 298, 311, 356, and 569 are not supported by the Provisional for which benefit is desired, therefore claims which recite these sequences are accorded priority only to the filing date of the instant application, of 4/28/1999. Applicant is advised, therefore, that claims 1-2, 10, 12, 16, 21, and 29 are granted priority to 4/28/1998. All other pending claims are granted priority only to 4/28/1999.

Claim Rejections - 35 USC § 101

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-2, 10-13, 15-22, and 24-31 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The specification discloses, on pages 67 *et seq.* that the inventive nucleic acids may be used to obtain nucleic acids from other species, to isolate promoters, to detect/identify polymorphisms, in genetic mapping, as molecular markers, to follow expression (e.g. to create an Expression Response), in hybridization experiments, and in tissue printing. These are all uses which are generic to the class of nucleic acids and are not specific, substantial and credible utilities for the SEQ ID NO's recited in the claims. With regard to hybridization and use to obtain sequences from other species, and use to obtain promoters, it is noted that any sequence identified as hybridizing or homologous to another is necessarily unique to the starting nucleic acid; however, a sequence which is similar or homologous to another sequence which itself has no known or established utility does not confer utility on the "finding" sequence.

While a promoter sequence, per se, may have a well-established utility, none of the claimed sequences are disclosed as being promoters. A use to FIND a promoter, when it is not disclosed/known whether a claimed sequence actually comprises such, is merely a "use" a to do further research. With regard to genetic mapping and use as a molecular marker, the specification does not disclose that the claimed sequences are known to localize to any gene/chromosome or have any other "molecular" trait which would make it useful in such assays. With regard to detection/identification of polymorphisms, known of the claimed sequences are disclosed as having a polymorphic site, or as being known to be associated with a polymorphism. In the absence of such a disclosure or knowledge present in the prior art, further research is required to determine if any of the claimed sequences comprises or is associated with a polymorphism or polymorphic site. Applicant is reminded that a "use" to do further research is not a specific, substantial and credible utility under 35 USC 101. With regard to an Expression Response and tissue printing, the specification discloses that the claimed sequences are isolated from various tissues of maize or soybean (Table A and pages 154-207), however, there is no disclosure that the claimed SEQ ID NO's are known to be specific to the particular tissue and/or developmental stage of plant from which they are isolated. There is no disclosure or evidence that expression of the claimed SEQ ID NO's are up-regulated, down-regulated, the sequences themselves turned "on" or "off', or that there is any other differential expression or regulation of or by the claimed sequences. Further experimentation would be required to determine what, if any, Expression Response or specific tissue expression can be attributed to any of the claimed SEQ ID NO's. therefore creation of an Expression Response or "use" in tissue printing is not a specific, substantial and credible utility. Because the utilities set forth above are not specific and/or substantial for the particular SEQ ID NO's claimed, and because further research would be required to determine if any of the asserted utilities MAY be

specific and substantial, the asserted utilities set forth above are not specific, substantial and credible with regard to any of SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, or 619.

The specification asserts on pages 1-2 that all of the inventive sequences encode enzymes involved in the phosphogluconate pathway, therefore an asserted utility for the claimed nucleic acids appears to be that based on the proteins encoded thereby. As previously set forth and reiterated herein (see below), the specification does not actually disclose that any of the claimed SEQ ID NO's is known to encode a protein or peptide, specifically one of the enzymes recited in the claims. Any nucleic acid molecule encoding an ATG codon could theoretically encode a peptide. However, it is well known in the art that a peptide is accurately and functionally expressed from a nucleic acid molecule only if an ORF is present; i.e. the "ATG" is read in the correct "frame" and there is a "stop" codon such that translation of the peptide starts and stops correctly. For the nucleic acid to have utility based on the peptide thus encoded, the peptide must have utility. That is, the identity and activity of the peptide must be known or established. A fragment of a protein, wherein the fragment itself does not have utility or activity, does not necessarily have a utility.

In the instant case, it is asserted that the claimed nucleic acid molecules encode phosphogluconate pathway enzymes or fragments thereof. Each nucleic acid molecule claimed has at least one (in most cases, several) ATG "codons". However, it is not known for ANY of the claimed sequences what the ORF is, therefore it is unknown whether any sequence is actually translated into a peptide, or, if translated, what the activity or function of that peptide may be. For example, SEQ ID NO: 14 comprises six "ATG" codons, but it is not known which, if any, is the start codon for a 6-phosphogluconate dehydrogenase. As set forth in the office action of 12/20/00, none of the claimed SEQ ID NO's appears to be long enough to encode the entirety of the enzyme disclosed by the specification to be putatively encoded thereby. It is possible that a claimed SEQ ID NO: encodes a fragment of an enzyme; however, it is not disclosed whether that fragment has activity or another function such that the fragment has utility under 35 USC 101.

As previously set forth, homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence. While the prior art teaches some nucleic acids with a degree of homology to the claimed sequences, and which encode phosphogluconate enzymes, the prior art does not teach that the elected SEQ ID's are known to encode the alleged proteins and the specification does not show that the peptides putatively encoded by the claimed nucleic acid sequences have an activity or function similar to those to which they are homologous.

As the instant specification does not disclose, and the prior art does not teach, that the instantly claimed nucleic acid sequences actually encode any protein or peptide, specifically the enzymes recited in the claims, the nucleic acid sequences represented by SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 do not have utility based on utility of a protein encoded thereby.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Claims 1-2, 10-13, 15-22, and 24-31 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 22, and 24-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

he claims are not enabled because neither the specification nor the prior art teach how to make the claimed enzymes from the SEQ ID NO's recited. Table A of the specification discloses that the claimed nucleic acid sequences encode the recited enzymes; however, it is again noted that homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence. As previously set forth and reiterated herein, the instant specification does not disclose anywhere that the claimed nucleic acids actually encode any peptide or protein. Also as previously set forth, while the prior art teaches isolated nucleic acid sequences which encode plant enzymes similar to those recited in the claims, the sequences taught by the prior art are not the same as those recited in the instant claims. As set forth above, each nucleic acid claimed comprises several ATG codons, any of which may be a possible start site for translation into a peptide, but no ORF has been disclosed as that encoding the claimed protein. It is known in the art that nucleic acids (genes) from eukaryotic organisms often comprise multiple open reading frames, (i.e. multiple start and/or stop codons), therefore one skilled in the art to must determine, for any given sequence, which open reading frame to use to generate a peptide. Given an amino acid sequence for a particular peptide, it would require fairly routine experimentation to "line up" the encoding polynucleotide with the peptide sequence to determine which portion of the nucleic acid sequence comprises the coding region for the peptide. The instant specification does not disclose any amino acids sequences. As no information which would allow one skilled in the art to determine how to generate the specific peptides used for the homology comparisons of Table A of the instant specification, it would require undue experimentation for one skilled in the art to determine how to generate the peptides, with the functionality claimed, from the disclosed nucleic acid sequences. The

specification does not disclose or point to information with regard to activity assays, which would also be necessary to determine if any expressed protein actually IS the enzyme recited.

The level of skill in the art is acknowledged to be high; however, as the one skilled in the art must "guess" at some information (e.g. open reading frames, actual start codon, homology parameters) and/or develop assays to arrive at the claimed invention, it would require undue experimentation for one skilled in the art to know how to make and use the claimed invention. For these reasons, the claims are not enabled.

35 U.S.C. 112, Written Description Rejection

Claims 1-2, 10-13, and 15-22 are again rejected, as previously set forth in the office actions of 12/20/00,12/4/01, 7/17/02, and 1/2/03, and new claims 24-30 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed 4/2/03 have been fully considered but they are not persuasive. Applicant's arguments are addressed below.

The specification discloses SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619. which putatively encode various phosphogluconate pathway enzymes. Sequences consisting of SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 meet the written description provisions of 35 USC 112, first paragraph. However, claims 1, 2, 10-22, 24-30 recite open claim language (comprising) and claims 1, 10, 24, and 26 are specifically directed to encompass sequences that hybridize to the claimed SEQ ID NO's. As the sequences recited in the claims are apparently fragments which do not appear to comprise ORF's or actually encode any known proteins, a nucleic acid "comprising" the fragments encompasses much larger sequences which may encode entirely different proteins from those recited, encompasses genomic sequences which may also comprise introns, noncoding regions, etc. In particular, a genomic sequence significantly longer in length than a claimed fragment may still hybridize to a recited sequence under the claimed conditions as introns, etc. may "bubble" out where mismatches occur but still allow for sufficient length of the genomic sequence to anneal under the claimed conditions. The specification sets forth a list of possible variations for the inventive sequences,

as argued by applicant, but does not actually describe, by sequence or structure, any of the variations, nor does the specification disclose any longer sequences (e.g. genomic) which may comprise the claimed sequences. For these reasons, the examiner maintains that the specification provides insufficient written description to support the genus encompassed by the claim.

Applicant argues that he need describe only the claimed invention, and insists that he has done so. In response, it is noted that while the claims do not specifically recite ORF's, at least claims 1-2, 22, 24, and 25 recite nucleic acids which encode proteins. It is well known in the art that an ORF is necessary for translation of any peptide, protein, or fragment thereof. As the claims recite encoding language, they are directed to nucleic acids which necessarily comprise ORF's. The specification does not disclose or describe an ORF for any nucleic acid, and therefore does not describe the claimed invention of at least claims 1-2, 22, 24, and 25.

Applicant argues that the specification describes gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, exogenous sequences, and so forth. In fact, the specification discloses that the inventive sequences may encompass gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, exogenous sequences, but does not actually describe, by sequence or structure, the sequences represented by gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, exogenous sequences, etc. anywhere. As previously set forth and reiterated above, gene sequences may comprise a variety of ORFs, exons, noncoding regions, repetitive sequences, etc., none of which are described by the instant specification. The specification does not describe or exemplify mutated sequences, SNPs, or polymorphic sequences comprising or comprised within the claimed SEQ ID NO's anywhere. It is generally accepted in the art that mutations and polymorphisms are somewhat unpredictable, both in sequence and frequency, therefore mere disclosure that a sequence MAY be mutated or comprise a polymorphism is not a description of the large variety of sequences embodied.

With regard to claims reciting hybridization language, it is not true, as argued by applicant, that every member of the genus embodied by the claims comprises a common structural feature; i.e. one of the claimed SEQ ID NO's. A long sequence with complementary regions interspersed by non-complementary regions (e.g. a gene comprising introns) may

hybridize to a claimed sequence wherein the non-complementary regions "bubble out", but sufficient length of the sequence complements a claimed SEQ ID NO: to meet the claimed hydridization conditions. Due to the interspersed non-complementary regions, the long sequence (gene) will NOT comprise the SEQ ID NO: to which it hybridizes. The specification fails to describe any sequence which does not consist of a claimed SEQ ID NO.

The examiner also maintains that the claimed sequences have not been shown to encode an entire enzyme, nor has any particular ORF been identified for the claimed sequences. The specification does not disclose that the any proteins have actually been translated and/or expressed from the claimed nucleic acid sequences, nor that any protein so expressed has been positively identified as one of the recited enzymes. Applicant acknowledges that BAKER et al. (Science (10/5/2001), vol. 294, pages 93-96) is directed to controversy in the art *in general* over prediction of function based on homology alone, but argues that the examiner does not "take into consideration Applicant's disclosure." AS previously set forth in various office actions, the examiner has closely examined the specification for any kind of support or evidence that the claimed nucleic acids actually do encode the recited proteins. Applicant has provided no evidence beyond that of the specification to show that the claimed nucleic acids encode the particular enzymes recited in the claims. Table A of the specification discloses sequence similarity information (e.g. % identity) between peptides putatively encoded by the claimed sequences and sequences which encode known enzymes, but does not disclose any comparison of binding regions, conserved regions, catalytic regions, etc. to support that the peptides putatively encoded by the claimed SEQ ID NO's would be expected to actually exhibit ANY enzyme activity. As previously set forth, BAKER teaches that structural (de novo) models are more accurate at predicting functional homologies between proteins, especially where sequence comparison fails (p. 94). Applicant argues that a detailed chemical structure; i.e. the claimed nucleic acid sequences are disclosed in the instant specification. While the nucleic acid sequences represented by the claimed SEQ ID NO's are fully described by the specification at the time of filing, nucleic acid sequences *encoding the proteins* recited in the claims were not fully described as set forth above. The specification does not disclose that the claimed nucleic acid sequences actually encode any proteins or peptides, as previously set forth and reiterated above, therefore nucleic acid sequences encoding the claimed proteins AND comprising the claimed SEQ ID NO's were not described in the specification as originally filed.

It is noted that while a nucleic acid sequence is a chemical structure, a nucleic acid "structure" is not the same as a peptide or protein structure, and is not necessarily predictive of a protein structure putatively encoded thereby. Given the acknowledged controversy in the art over whether sequence similarity alone can be used to accurately predict function, and the lack of teaching in the specification for whether any of the claimed nucleic acids actually encodes any protein, specifically one of the recited enzymes, and absent factual evidence to the contrary, one skilled in the art would reasonably doubt that sequence similarity alone is sufficient to predict whether the biological and enzymatic activity of the claimed subject matter is the same as that of the prior art. The specification fails to describe ANY nucleic acid actually encoding one or more of the claimed enzymes, therefore the rejection is maintained.

With the exception of sequences consisting of SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. For all of the reasons set forth above and previously set forth, the rejection is maintained and new claims 24-30 are rejected.

Claims 1, 22, 24, and 25 recite a "substantially purified nucleic acid" which encodes a "maize or soybean phosphogluconate pathway enzyme" wherein the nucleic acid is a specific SEQ ID NO: or hybridizes to specific SEQ ID NO's. The specification fails to describe any "substantially purified nucleic acid sequence" which is known to encode a maize or soybean phosphogluconate pathway enzyme. Once purified, nucleic acid and peptide sequences do not carry information with regard to their origin. An enzyme expressed from a nucleic acid will display activity, under appropriate conditions, no matter what system, cell line, clone, etc. it is expressed from/in. A purified sequence (comprising a complete ORF) may be cloned into another plant/cell line and a protein expressed; is the protein still a "maize or soybean" enzyme? In addition, it is noted that sequences which hybridize to one of the claimed nucleic acids under the conditions recited, and encode one of the recited enzymes, but are NOT sequences purified from maize or soybean are known in the art (see e.g. the sequence taught by MARTIN et al., set forth in the previous office action). As the specification fails to describe a "substantially purified nucleic acid" which encodes a "maize or soybean" enzyme, the rejection

of claims 1 and 22 for lack of written description is maintained and claims 24-25 are newly rejected.

Conclusion

Claims 1-2, 10-13, 15-22, and 24-31 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

Marjorie A. Moran

MARJORIE MORAN
PATENT EXAMINER

mam
June 14, 2003